Armed Forces College of Medicine

AFCM

Mycobacteria

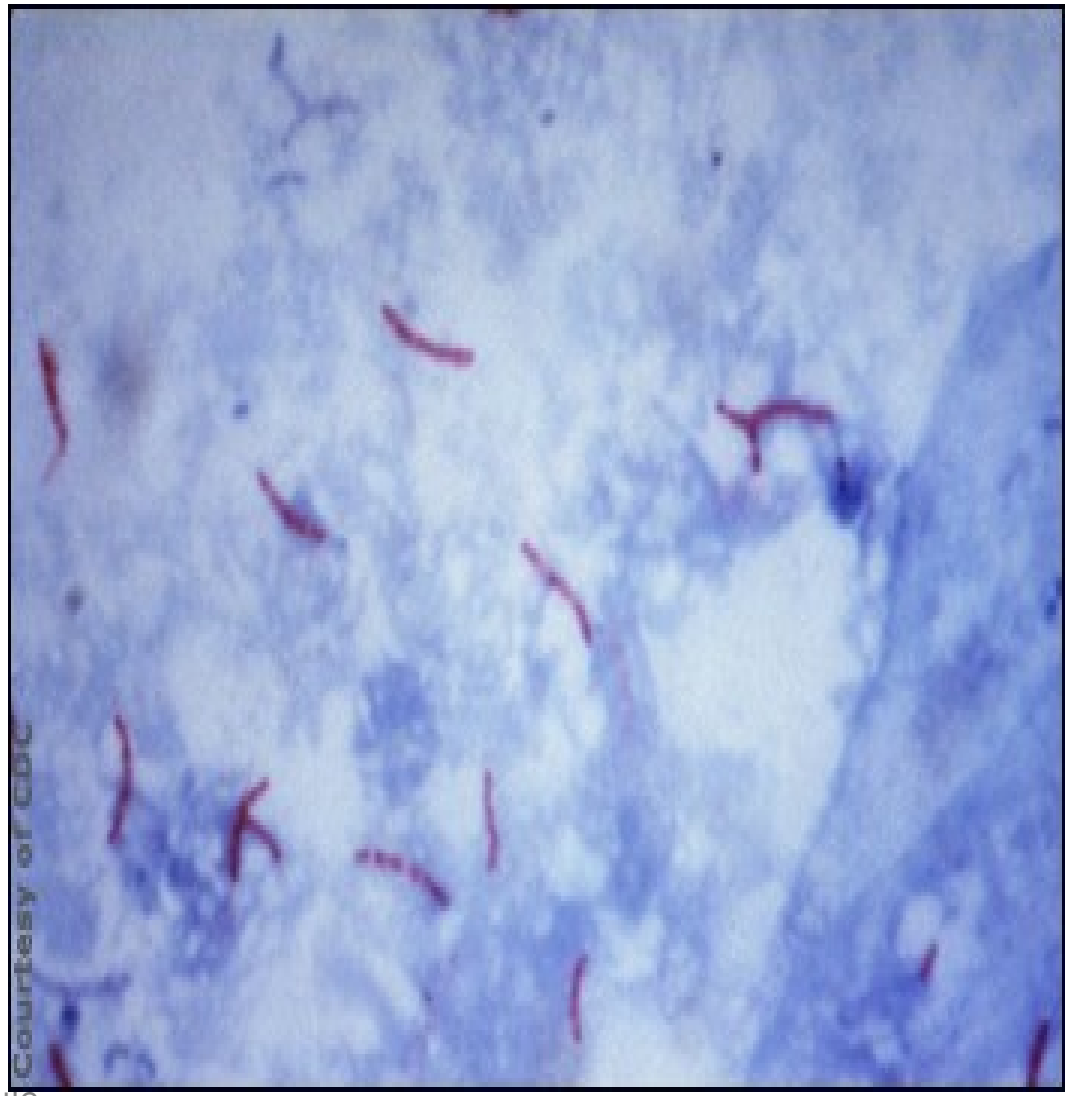
Intended Learning Objectives (ILOs)

By the end of this lecture the student will be able to:

- Describe pathogenesis & clinical manifestations of pulmonary TB
- Outline the laboratory diagnosis of T.B.

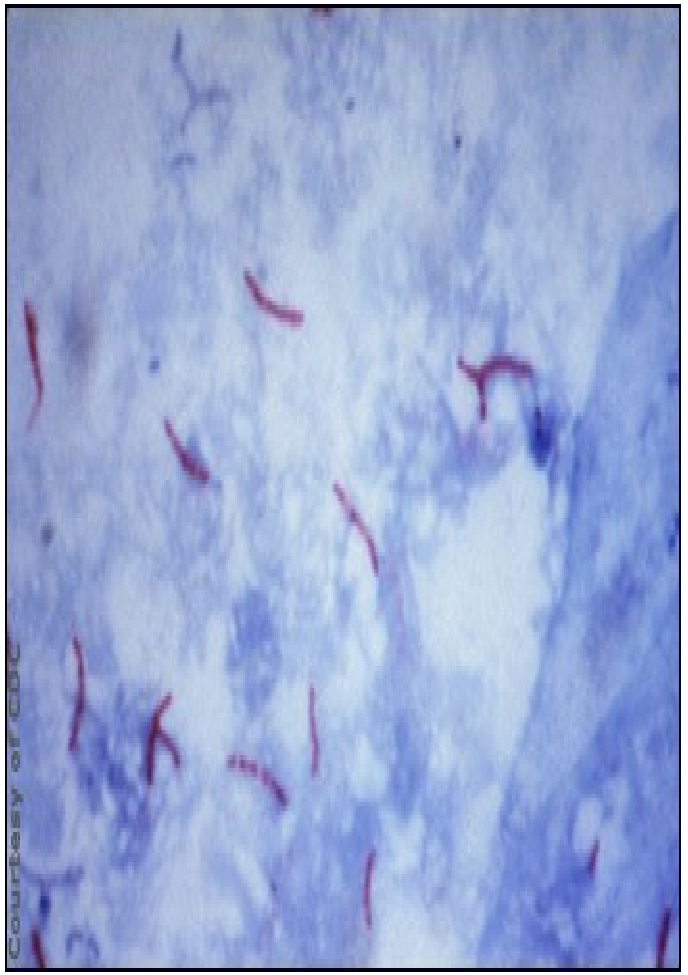
Mycobacteria

Mycobacteria are aerobic bacilli that have an unusual cell wall, resulting in their inability to be Gram-stained.

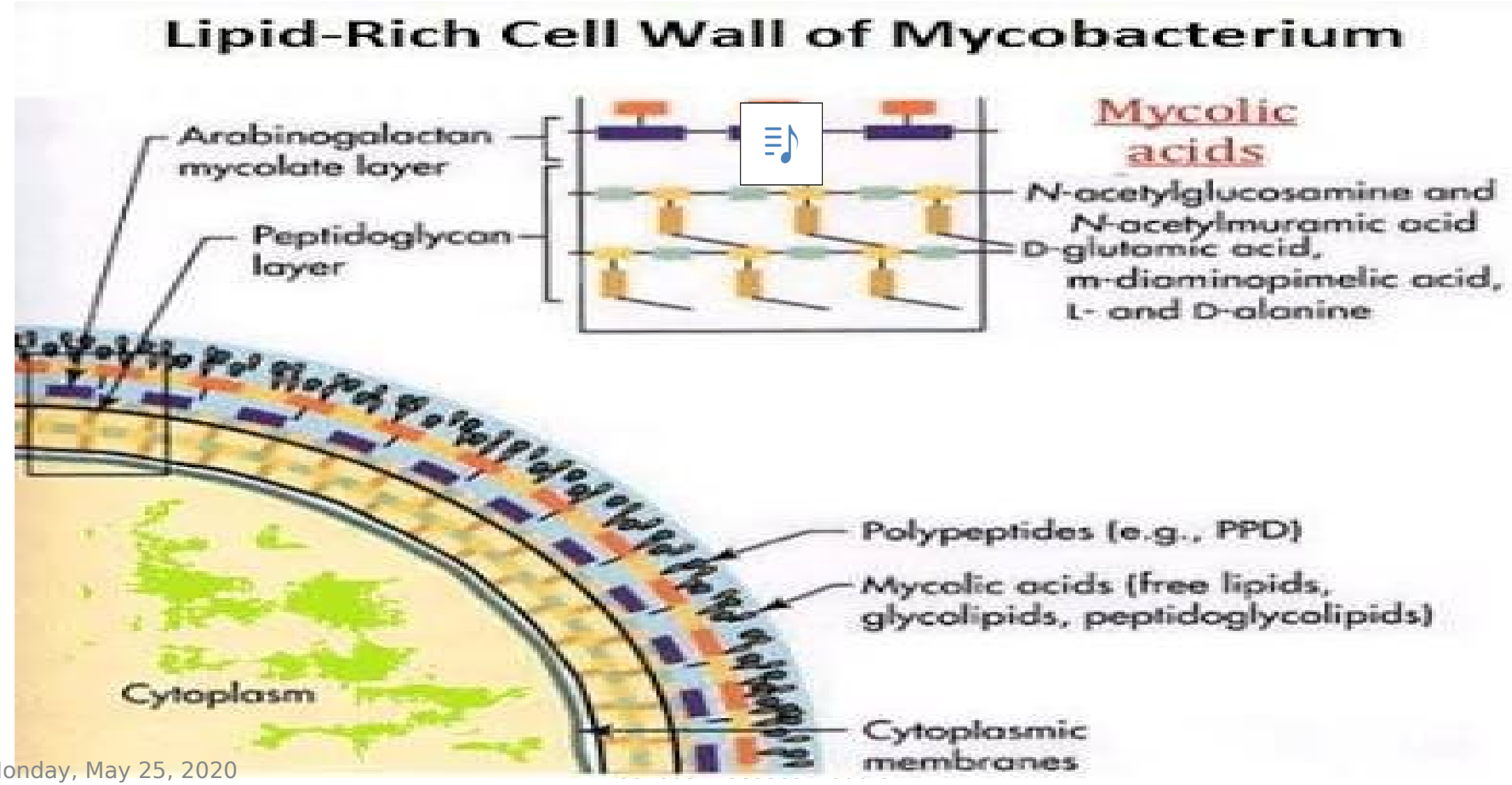


Mycobacteria

These bacteria are ACID FAST because they resist decolorization with acid/ alcohol after being stained with carbol fuchsin. This is due to the high concentration of lipids, mycolic acids, in their cell wall



Cell wall of Mycobacteria



Members of Mycobacteria

Mycobacterium tuberculosis complex

*Mycobacterium tuberculosis (human)
*Mycobacterium bovis (cattle)

Atypical mycobacteria (MOTTs)

*Widespread in the environment
*Some are antigenically similar to M. tuberculosis
*Causes T.B. like disease and granulomas in Immuno-compromised patients

Mycobacterium leprae leprosy

Mycobacterium tuberculosis- Disease

- This organism causes tuberculosis.
- Worldwide, M. tuberculosis causes more deaths than any other single microbial agent.
- One-third of the world's population is infected with this organism

cobacterium tuberculosis- Propertie

- M. tuberculosis is an obligate aerobe disease in highly oxygenated tissues (upper lobe of the lung and the kidney)

- Non motile non-capsulated and non-spore forming

cobacterium tuberculosis- Propertie

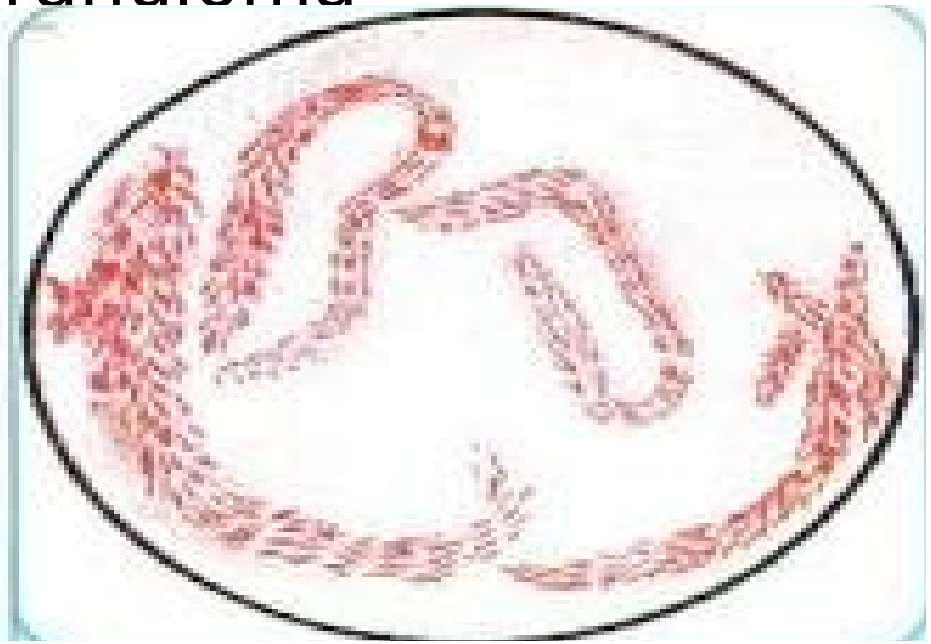
- Resistant to dehydration survives in dried expectorated sputum
- Grows slowly

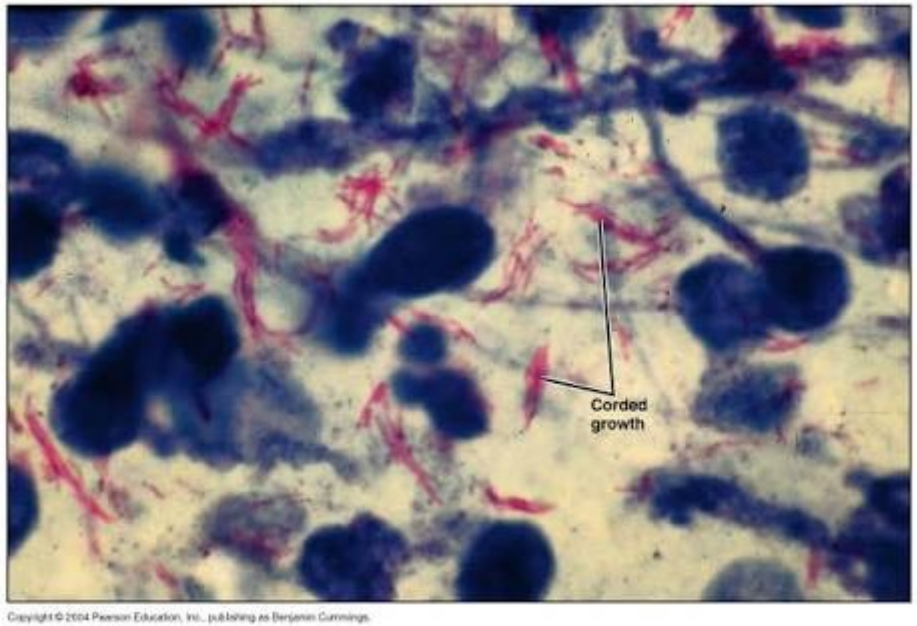
Cultures incubated for 6 to 8 weeks before recording as negative

Prolonged course of TTT

cobacterium tuberculosis- Virulence factors

1- Cord factor (glycolipid): Virulent strains grow in a characteristic “serpentine” cordlike pattern, as the bacilli stick together toxic to leukocytes+ antichemotactic+ development of granuloma





cobacterium tuberculosis- Virulence factors

2- Several antigenic proteins elicit hypersensitivity reactions

3- Mycolic acid: inhibits formation of phagolysosome in macrophage→ INTRACELLULAR SURVIVAL.

4- Metabolically inactive: difficult to kill by antibiotics

5- Antibiotic resistance: acquired by chromosomal gene mutation.

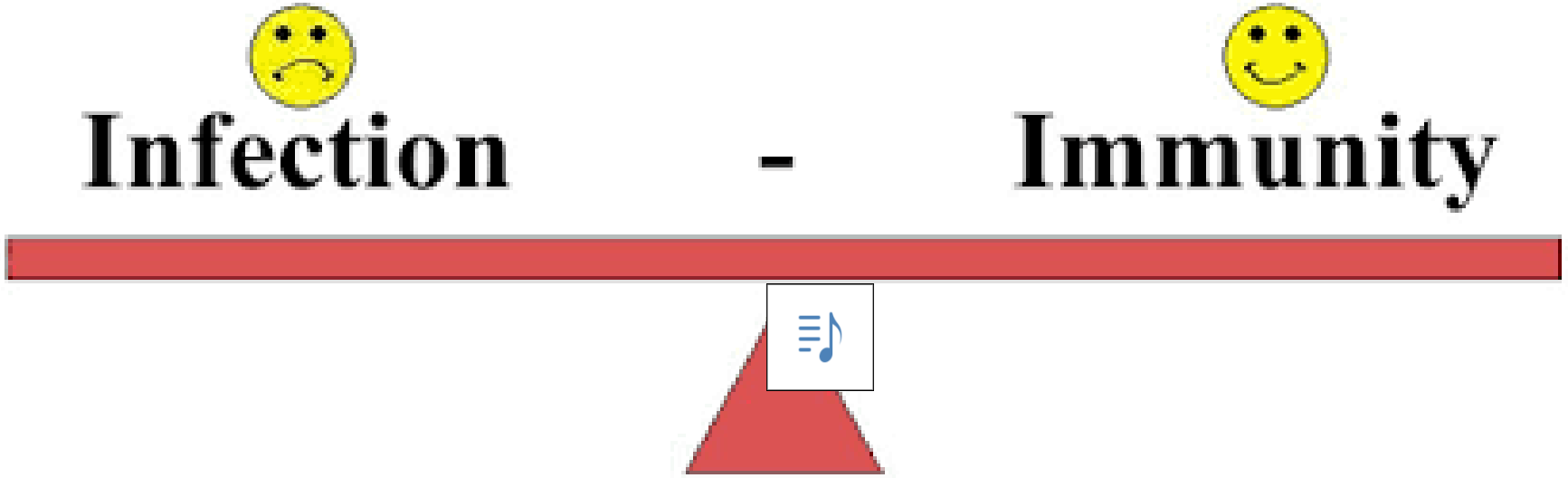
cobacterium tuberculosis- Transmission

Mycobacterium tuberculosis	Mycobacterium bovis
• Person to person by respiratory AEROSOLS (mostly from smear positive patients) Lung reside in MQ. • Humans are natural reservoir	• Ingestion of unpasteurized milk from infected cows intestinal tuberculosis

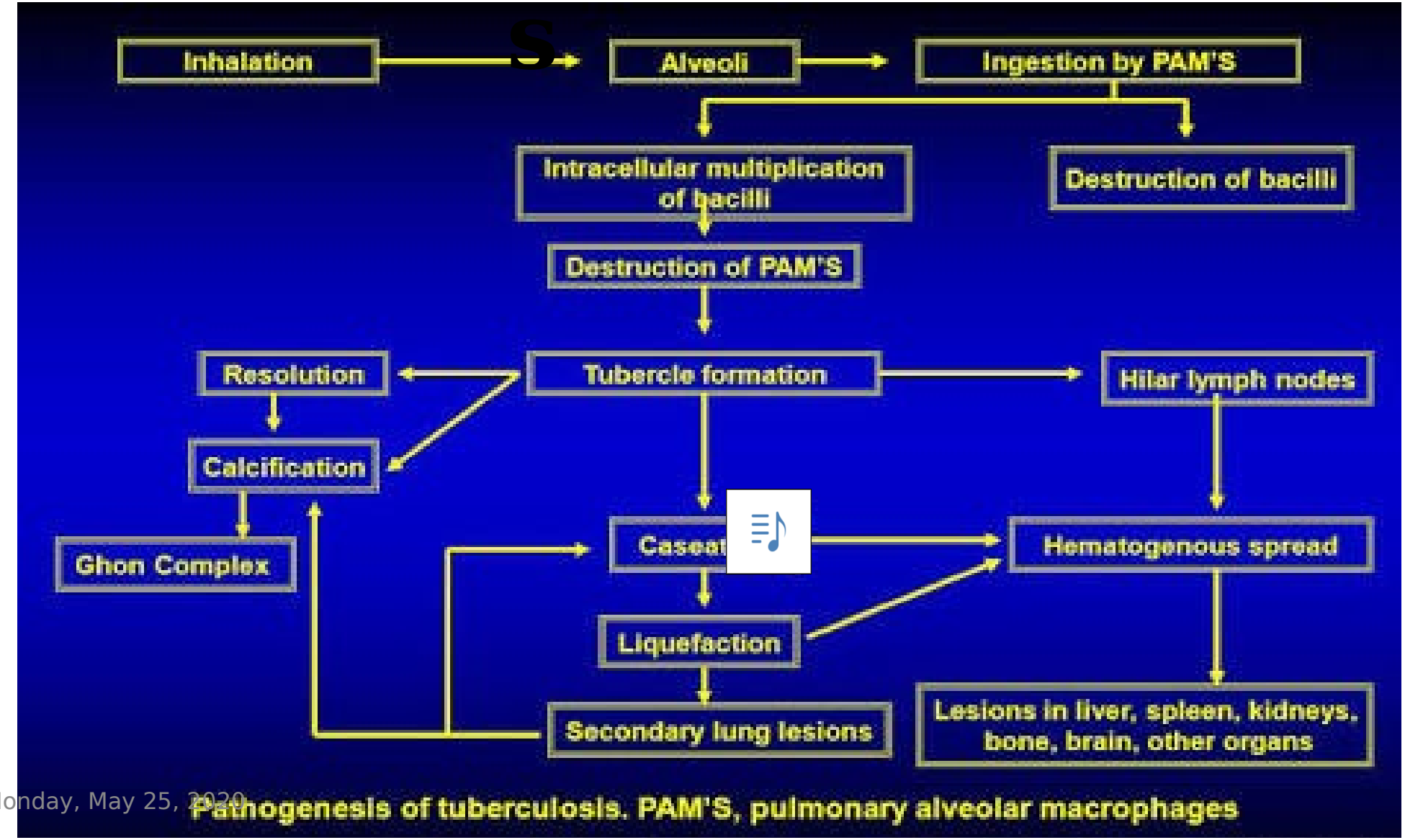
Risk factors: Immune suppression, poor housing, poor nutrition

Pathogenesis

- NO exotoxin… NO endotoxin
- MQ infection phagosome mycolic acid inhibits its fusion with lysosomes the organism escapes the degrading lysosomal enzymes Intracellular survival.



Pathogenesi



Pathogenesis

Spread of the organism within the body occurs by two ways:

Tubercle erodes into a bronchus, empties its caseous contents spread of the organism to other parts of the lungs, to the GIT if swallowed, and to other persons if expectorated

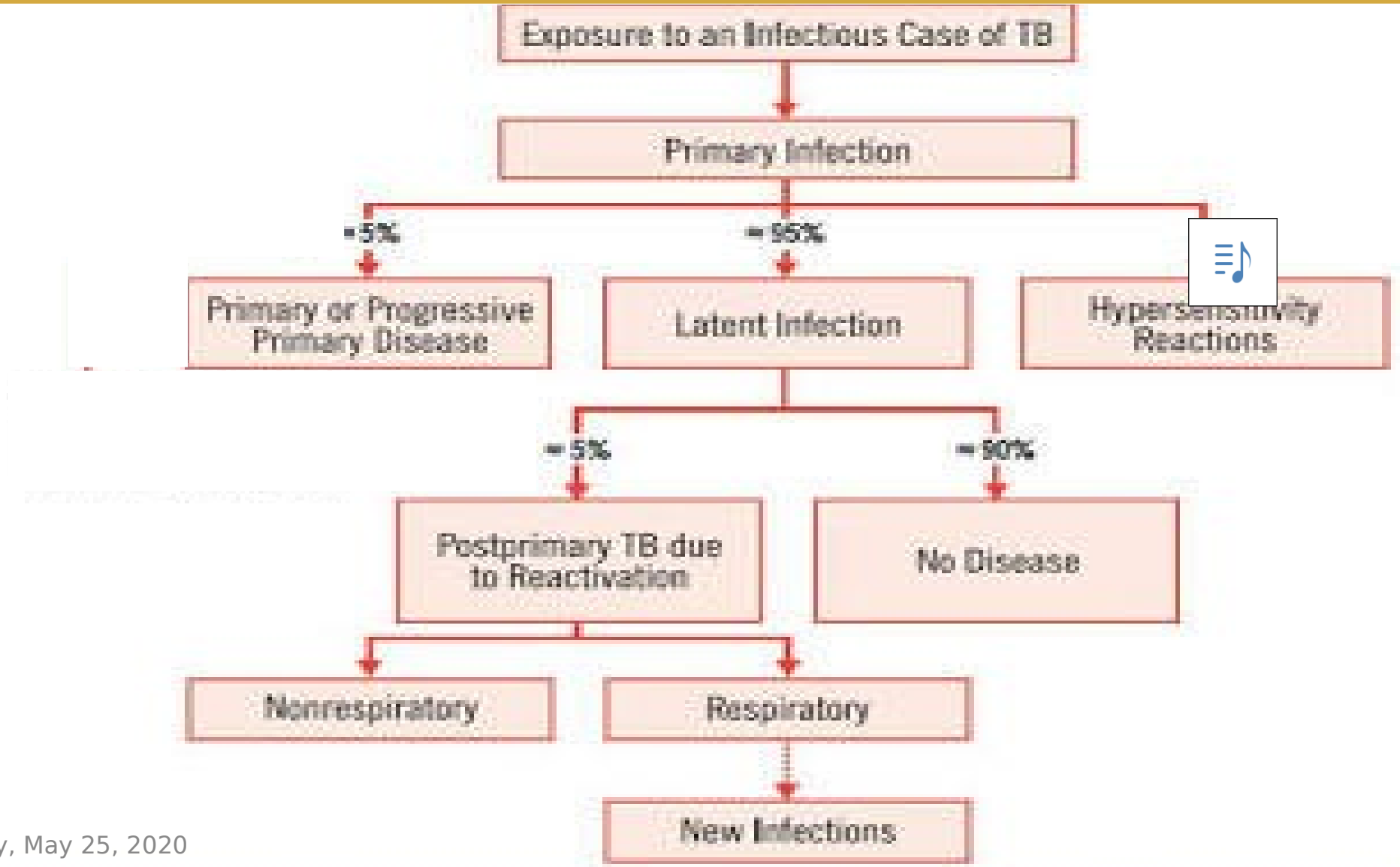
Via the bloodstream to many internal organs if cell-mediated immunity fails to contain the initial infection or at a late stage if a person becomes immuno-compromised

Immunity and Hypersensitivity

- After recovery from the primary infection, resistance to the organism is mediated by Th-1

- Circulating antibodies also form. Do they have a role in resistance??

Clinical findings



Clinical findings

- Asymptomatic: Latent infection…
- Generally: fever, night sweating, weight loss
- Pulmonary: cough, expectoration.. Hemoptysis??
- Extrapulmonary: lymphadenitis (most common), erythema nodosum

Clinical findings

- GIT: abdominal pain and diarrhea, intestinal obstruction or hemorrhage may occur.

- Oropharyngeal tuberculosis: painless ulcer + lymphadenopathy

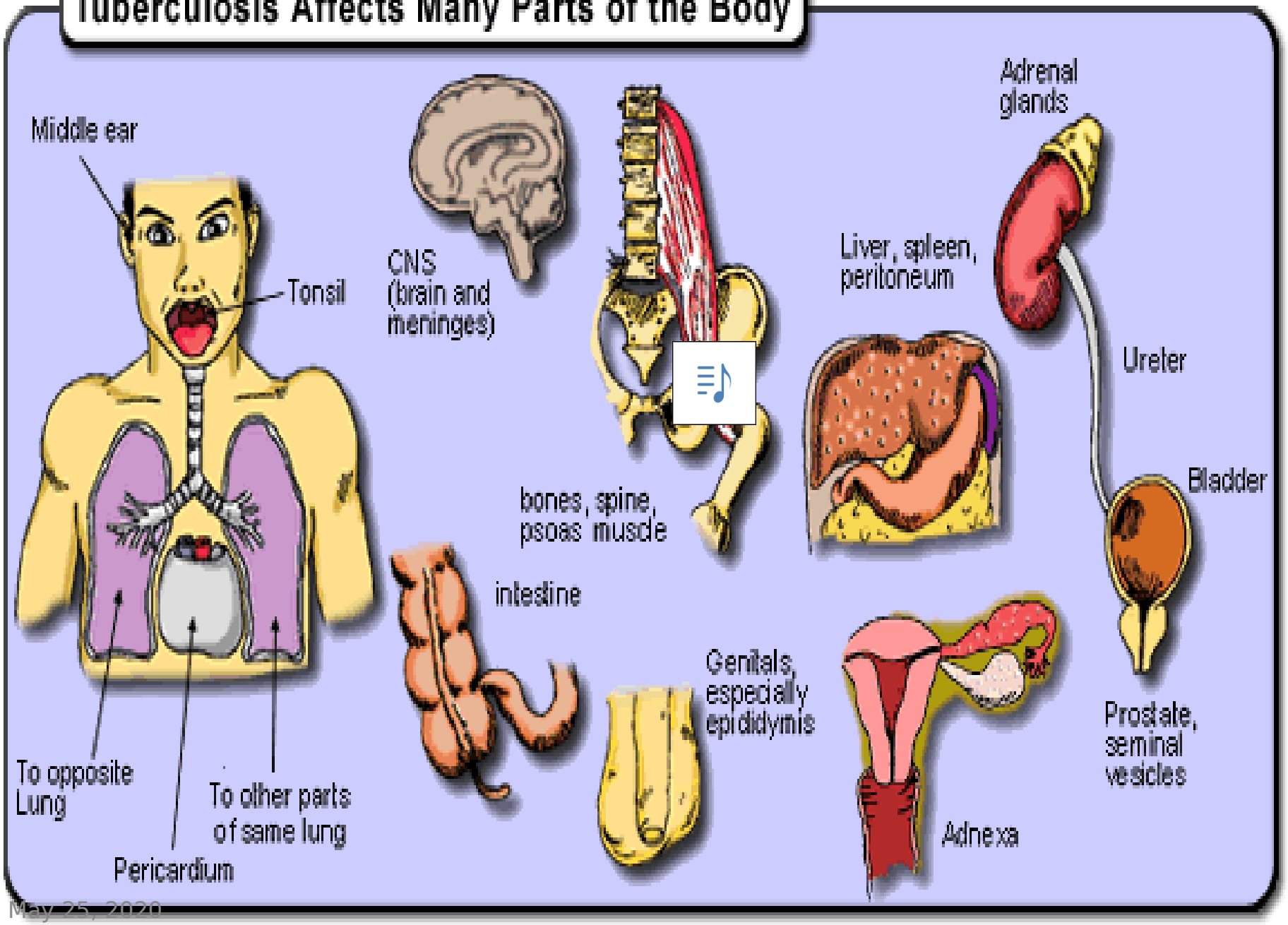
Clinical findings

- Renal tubercuolsis: mostly reactivation lesion dysuria, hematuria, and flank pain occur. “Sterile pyuria” is a characteristic finding????
- Miliary T.B.: multiple disseminated lesions resembling millet seeds

Tuberculous meningitis and tuberculous osteomyelitis, specially vertebral osteomyelitis (Pott’s dis

are important disseminated forms.

Tuberculosis Affects Many Parts of the Body



Laboratory Diagnosis

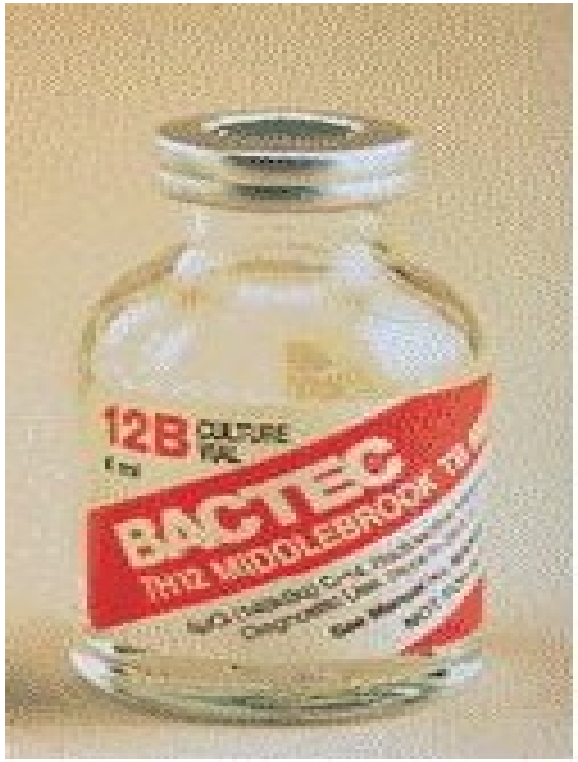
1- Acid fast staining of sputum or other specimens by ZN stain

2- Isolation and identification: culture is performed on L.J. medium incubated for up to 8 weeks

- In liquid BACTEC medium, radioactive metabolites are present, and growth can be detected by the production of radioactive carbon dioxide in about 2 weeks. OBSOLETE

3- PCR and nucleic acid amplification techniques: detect the presence of M. tuberculosis directly in clinical specimens

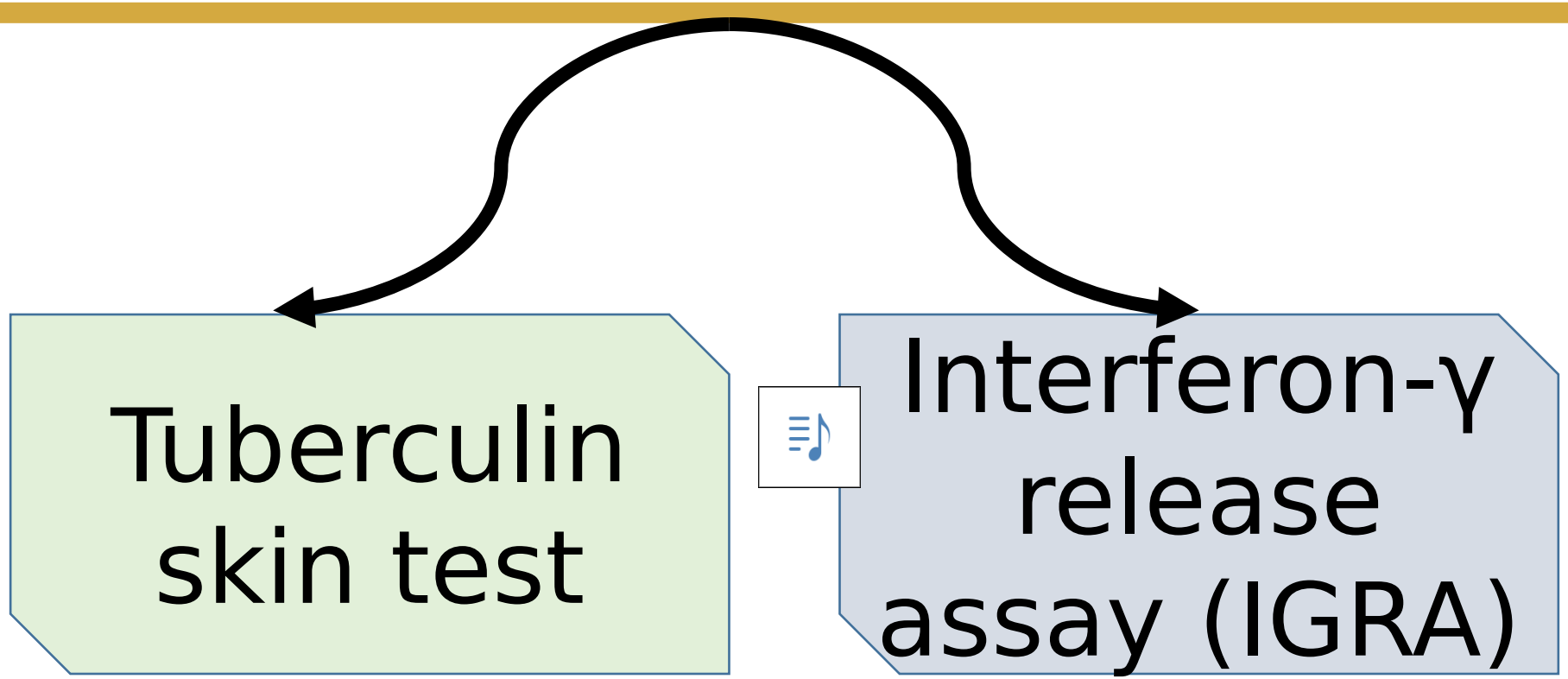
Specimen containing TB



Utilize ^{14}C labeled palmitic as a single carbon source

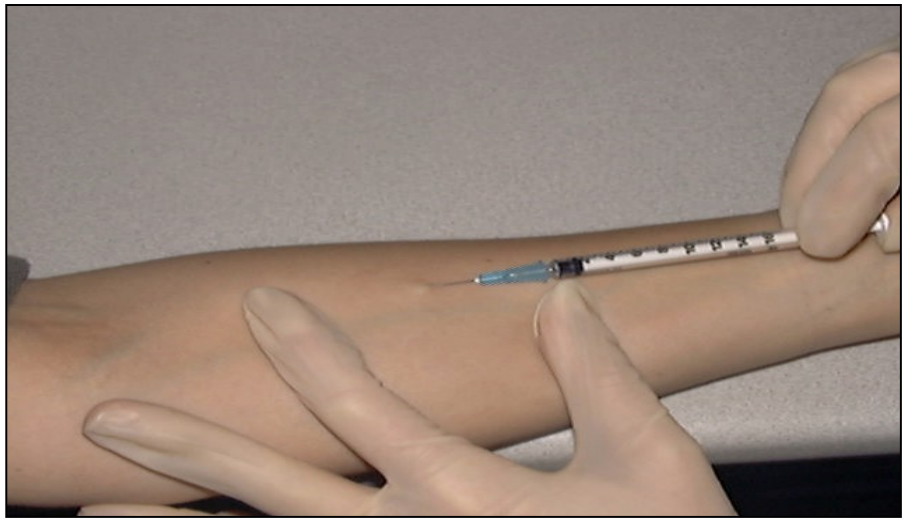
Radioactive CO_2

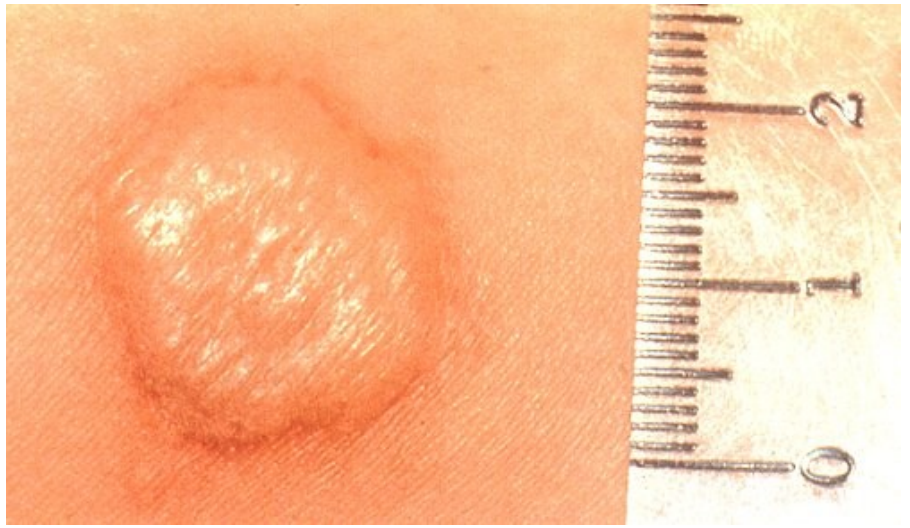
Laboratory Diagnosis of Latent T.B.



Tuberculin skin test

Purified protein derivative (PPD) is the antigen used injected intra-dermally delayed hypersensitivity reaction within 72 hours induration surrounding the test site measuring its diameter which depends on the status of the individual being tested





Tuberculin skin test

- The test is considered positive when the diameter is:

15 mm or more

- In a person who has no known risk factors

10 mm or more

- In a person with high-risk factors, (homeless person, intravenous drug users, medical staff.

5 mm or more

- In a person who has deficient cell-mediated immunity (e.g. AIDS patients) or close contact with a person with active tuberculosis

Tuberculin skin test

- A positive skin test result indicates previous exposure to the organism but not necessarily active disease.
- The tuberculin test becomes positive 4 to 6 weeks after infectio

Interferon-γ release assay (IGRA)

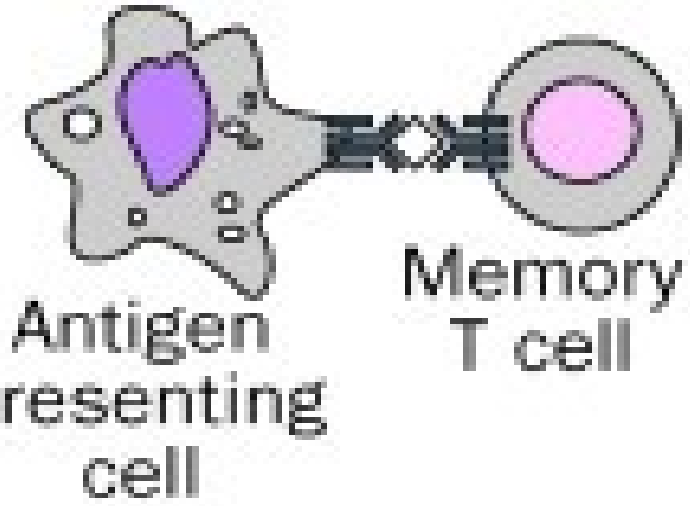
Blood cells from the patient are exposed to antigens from M. tuberculosis (in vitro test)

**This antigen is NOT PRESENT in BCG

Amount of interferon-γ released from the cells is measured

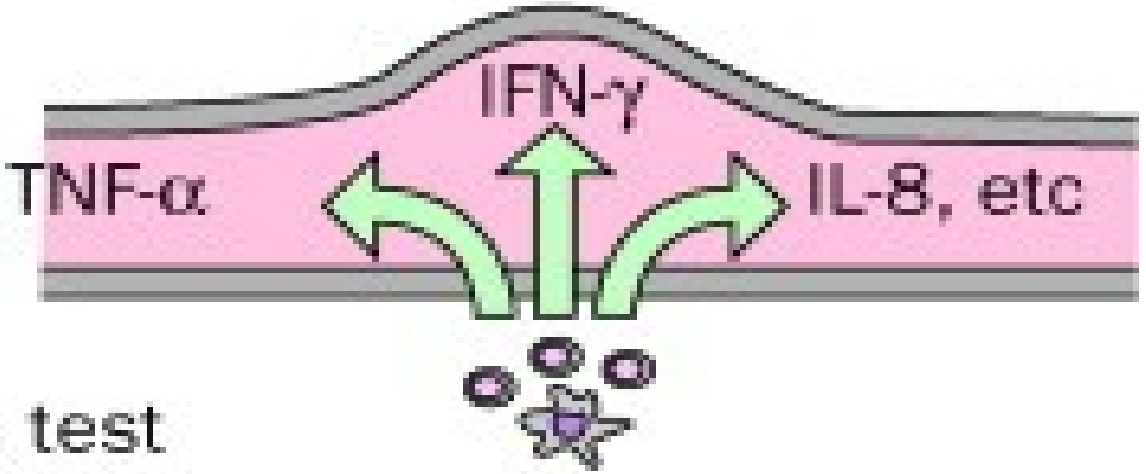
Advantages??

Presentation of mycobacterial antigens

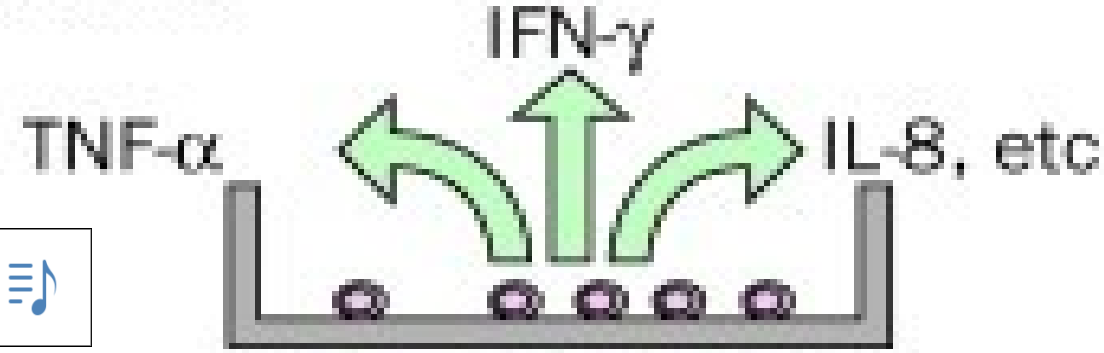


Skin test

Measurement of induration and erythema



in-vitro blood test



Measurement of IFN-γ production

Emergence of T.B.

- Tuberculosis emerging today as a leading infectious killer of youth and adult all over the world:

1- Increased incidence of HIV infection.

2-Emergence of MDR strains.

3- ⟶

Prevention of T.B.

1- BCG vaccine: induces partial resistance to tuberculosis. Does not prevent disease. Prevents mortality in children under 5 years of age.

The vaccine contains a strain of live-attenuated M. bov called Bacillus Calmette-Guérin.

- Effectiveness ranges from 0% to 70%.

2- Pasteurization of milk prevents intestinal T.B.

3- To prevent spread to medical personnel, other patients and the environment: Airborne isolation precautions

4- Tuberculin skin test to detect recent converters in: people with HIV infection, close contacts of patients with active tuberculosis, alcoholics and intravenous drug users. HCWs exposed to patients